More Frequent Hospitalizations and Worse Quality of Life with Late Right Heart Failure Compared to Early Right Heart Failure after LVAD as DT

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Disclosures

Jeffrey Teuteberg MD: Consultant – Medtronic, CareDx, Abiomed, Abbott; Speaking – Medtronic, CareDx, Paragonix

William Hiesinger MD: None

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Background

Right Heart Failure in LVAD Patients

- Right heart failure (RHF) is a common adverse event (AE) following left-ventricular assist device (LVAD) implantation in destination therapy (DT) patients
- Timing of RHF may have differential impact on outcomes, AEs, and functionality
- Late right heart failure (LRHF) is not well characterized in DT HVAD population

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Background

HVAD DT Trials

ENDURANCE[1]

- Prospective, randomized, multicenter trial comparing the safety and efficacy of HVAD to HMII (control) in end-stage heart failure patients who did not qualify for heart transplant.
- Enrollment 446 patients
  - Randomized 2:1 to HVAD or HMII
  - **296 HVAD System**
  - 149 HMII

ENDURANCE Supplemental[2]

- Prospective, randomized, multicenter trial to prospectively determine the effectiveness of a blood pressure management strategy on neurological injury in DT patients receiving the HVAD System vs HMII (control).
- Enrollment 465 patients
  - Intent-to-treat population randomized 2:1 HVAD or HMII
  - **308 HVAD System**
  - 157 HMII

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1. Rogers, et al. 2017. *N Engl J Med.*
2. Milano, et al. 2018. *JACC Heart Fail.*

Purpose

- To assess the incidence of RHF, ERHF, and LRHF in the HVAD population using pooled data from the ENDURANCE and ENDURANCE Supplemental trial
- Risk factors and outcomes of ERHF have been extensively reported
- An understanding of LRHF is less well established, so this report focuses on the risk factors, adverse events, survival, quality of life, and functional capacity of DT patients suffering LRHF

Methods

- Post-hoc analysis of all DT HVAD patients enrolled in ENDURANCE and ENDURANCE Supplemental Trials (n=604)
- Patients who experienced RHF through 2 years were examined with a focus on patients who developed LRHF
- Baseline characteristics, as well as adverse events, survival, quality of life, and functional capacity through 2 years post-HVAD implant were analyzed

Methods

RHF definitions

RHF was defined as requiring *at least one* of the following:

- Right ventricular assist device (RVAD) implant
- Inhaled nitric oxide for > 1 week
- Inotropic therapy for > 1 week

Patients with RHF were categorized into 2 groups based on timing of RHF onset

1. **Early RHF** (ERHF): RHF during VAD implant hospitalization
2. **Late RHF** (LRHF): RHF during surveillance periods (3, 6, 12 months and every 6 months post-implant thereafter)

Results – RHF with HVAD

DT HeartWare™ HVAD™ System and RHF

- **ENDURANCE trial (DT1) with HVAD (PY: 410.04)**
  - RHF: 0.32 EPPY*
  - RHF requiring RVAD: 0.02 EPPY
- **ENDURANCE Supplemental trial (DT2) with HVAD (PY: 454.86)**
  - RHF: 0.28 EPPY
  - RHF requiring RVAD: 0.02 EPPY
- **Combined DT1 + DT2 with HVAD (PY: 864.9)**
  - RHF: 0.30 EPPY
  - RHF requiring RVAD: 0.02 EPPY

** EPPY = events per patient year*

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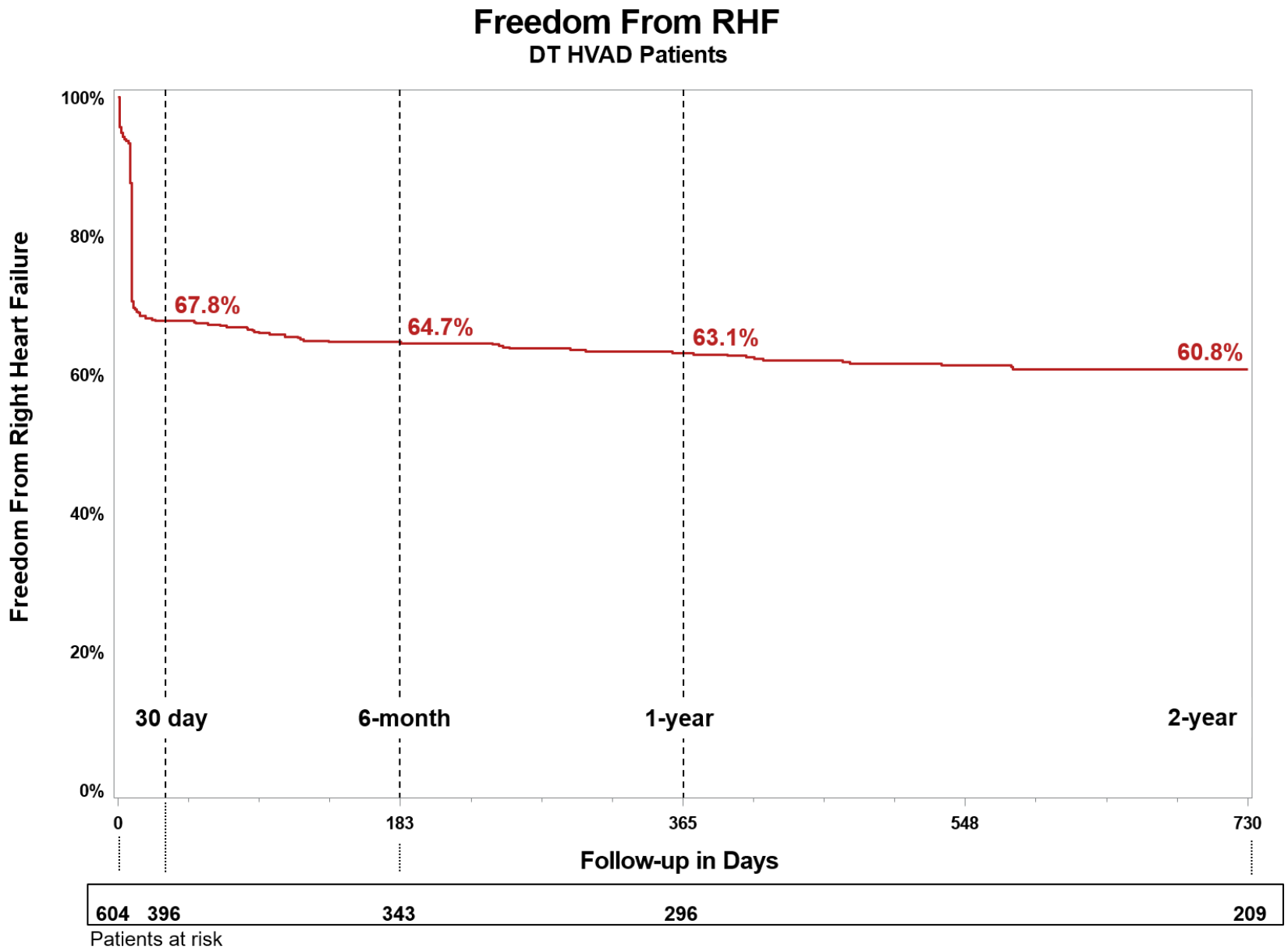
Results

ERHF & LRHF

- **Early Right Heart Failure**
  - 176 (29.1%) patients had RHF during the VAD implant hospitalization
    - 4 (2.3%, 0.04 EPPY) required RVAD implant
    - Median time to ERHF was 9 days
- **Late Right Heart Failure**
  - Total 53 (8.8%) of patients
    - LRHF only: 33 (5.5%) RHF post-VAD implant hospitalization
    - ERHF & LRHF: 20 (3.3%) patients with ERHF and RHF post-VAD implant hospitalization
  - LRHF criteria:
    - 0% RVAD implant
    - 0% iNO
    - 100% inotropes > week
  - Median time to LRHF was 222 days, range 55 to 715 days

Results

Freedom from All RHF



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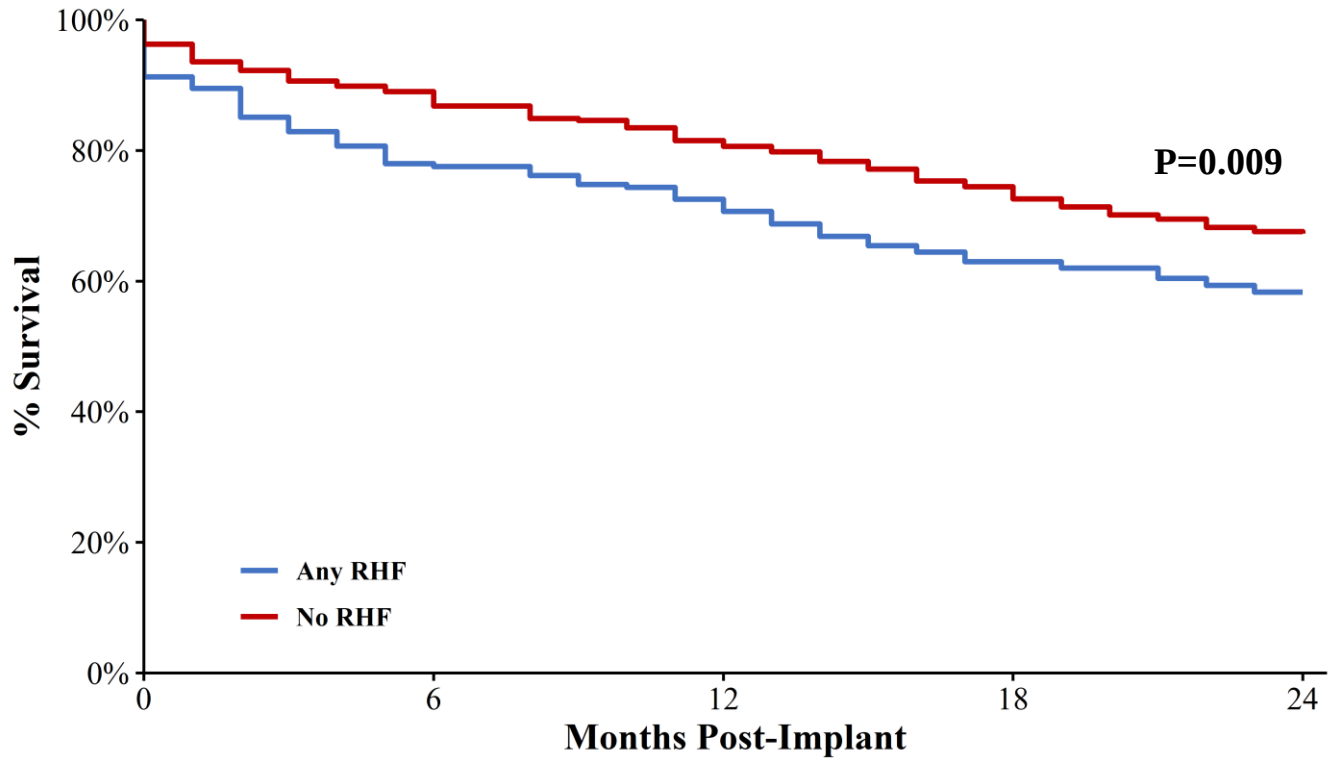
Results

Kaplan-Meier Survival (All RHF vs No RHF)



Number at risk

229	173	156	128	110
375	325	286	243	210

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Results

Baseline Characteristics (Any Late RHF vs No RHF)

When compared to patients without RHF, patients experiencing Late RHF had

- Larger BMI (29.4 vs 27.6, p=0.04)
- Lower AST (27.5 vs 32.3, p=0.01)
- Lower PAPi (2.5 vs 4.0, p=0.001)
- Less severe MR
  - None-Mild (51.9% vs 40.3%, p=0.01)
  - Mod-Severe (40.4% vs 58.9% p= 0.02)
- Longer index hospital length of stay (29.7 vs 21.0 days, p<0.0001)

	Late RHF (n=53)	No RHF (n=375)	p-value
Age (years)	61.8 +/- 10.9	64.3 +/- 11.1	0.13
Body Mass Index (kg/m^2)	29.4 +/- 6.7	27.6 +/- 5.7	**0.04**
Male	75.5%	81.9%	0.26
White	67.9%	78.4%	0.15
Black	32.1%	18.4%	
Creatinine (umol/L)	128.0 +/- 43.4	124.1 +/- 38.5	0.50
Blood Urea Nitrogen (mmol/L)	10.0 +/- 4.4	10.4 +/- 5.5	0.65
Total Bilirubin (umol/L)	17.5 +/- 13.2	18.1 +/- 11.6	0.75
Aspartate Transaminase (U/L)	27.5 +/- 11.0	32.3 +/- 19.2	**0.01**
Alanine Transaminase (U/L)	31.5 +/- 28.3	34.1 +/- 28.6	0.54
Smoking	62.3%	69.9%	0.27
Diabetes	49.1%	48.3%	>0.99
Peripheral Vascular Disease	9.4%	11.7%	0.82
Chronic Obstructive Pulmonary Disease	28.3%	23.7%	0.49
Carotid Artery Disease	15.1%	15.7%	>0.99
Stroke/TIA	26.7%	16.0%	0.19
Ischemic Heart Failure	58.5%	58.7%	0.96
Cardiac index (L/min/m^2)	2.2 +/- 0.5	2.2 +/- 0.7	0.90
Pulmonary Capillary Wedge pressure (mmHg)	21.6 +/- 7.8	21.5 +/- 7.7	0.93
Mean Pulmonary Artery Pressure (mmHg)	32.6 +/- 8	32.7 +/- 9.9	0.98
Central Venous Pressure (mmHg)	10.3 +/- 3.8	10.2 +/- 6.2	0.93
Pulmonary Vascular Resistance (Wood)	2.6 +/- 1.2	2.9 +/- 3.9	0.41
Mean Arterial Pressure (mmHg)	78 +/- 11.2	78.6 +/- 11.3	0.71
Right Ventricular Stroke Work Index	0.7 +/- 0.2	0.6 +/- 0.3	0.33
Pulmonary Artery Pulsatility Index	2.5 +/- 1.3	4.0 +/- 3.3	**0.001**
Left Ventricular Ejection Fraction	16.4 +/- 5.3	17.5 +/- 4.8	0.11
Tricuspid Regurgitation			
None-Mild	51.9%	60.5%	0.29
Mod/Severe	46.2%	37.9%	0.29
Mitral Regurgitation			
None-Mild	59.6%	40.3%	**0.01**
Mod/Severe	40.4%	58.9%	**0.02**
Aortic Insufficiency			
None-Mild	88.5%	92.8%	0.27
Mod/Severe	7.7%	2.4%	0.06
Aortic Repair/Replace	3.8%	5.3%	>0.99
Mitral Repair/Replace	5.7%	4.8%	0.73
Tricuspid Repair Replace	11.3%	17.3%	0.33
Intermacs 1	3.8%	3.2%	
Intermacs 2	17.0%	29.7%	0.22
Intermacs 3	54.7%	42.0%	
Intermacs 4-7	24.5%	25.1%	
Length of Hospital Stay (days)*	29.7 +/- 18.3	21.0 +/- 12.2	**<0.0001**

*Conditional on discharge

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Results

Adverse Events (Any Late RHF vs No RHF)

Compared to patients without RHF through 2 years of VAD support, Late RHF patients had higher rates of:

- Hepatic dysfunction (0.06 vs 0.01 EPPY, p=0.0004)
- Sepsis (0.13 vs 0.06 EPPY, p=0.04)
- Acute Renal Dysfunction (0.10 vs 0.01 EPPY, p=0.001)
- Respiratory Failure (0.15 vs 0.03 EPPY, p=0.0003)
- Rehospitalizations (3.46 vs 2.13 EPPY, p<0.0001)

Adverse Event	Late RHF (n=53) (PY: 78.31)	No RHF (n=375) (PY: 566.48)	p-value
Bleeding	0.52	0.48	0.06
GI Bleed	0.26	0.33	0.48
Cardiac Arrhythmia	0.23	0.20	0.58
Ventricular Arrhythmia	0.17	0.12	0.15
Any Suspected Pump Thrombosis	0.05	0.05	0.77
Hepatic Dysfunction	0.06	0.01	**0.004**
Infection	0.65	0.52	>0.99
Sepsis	0.13	0.06	**0.04**
Driveline Exit Site	0.10	0.15	0.33
Stroke	0.08	0.13	0.52
Ischemic CVA	0.05	0.10	0.45
Hemorrhagic CVA	0.03	0.03	>0.99
TIA	0.05	0.04	>0.99
Renal Dysfunction	0.11	0.02	**0.0003**
Acute	0.10	0.01	**0.001**
Chronic	0.01	0.00	0.23
Respiratory Failure	0.15	0.03	**0.0003**
All Cause Rehospitalization	3.46	2.13	**<0.0001**

Legend GI: gastrointestinal; CVA: cerebrovascular accident; TIA: transient ischemic attack

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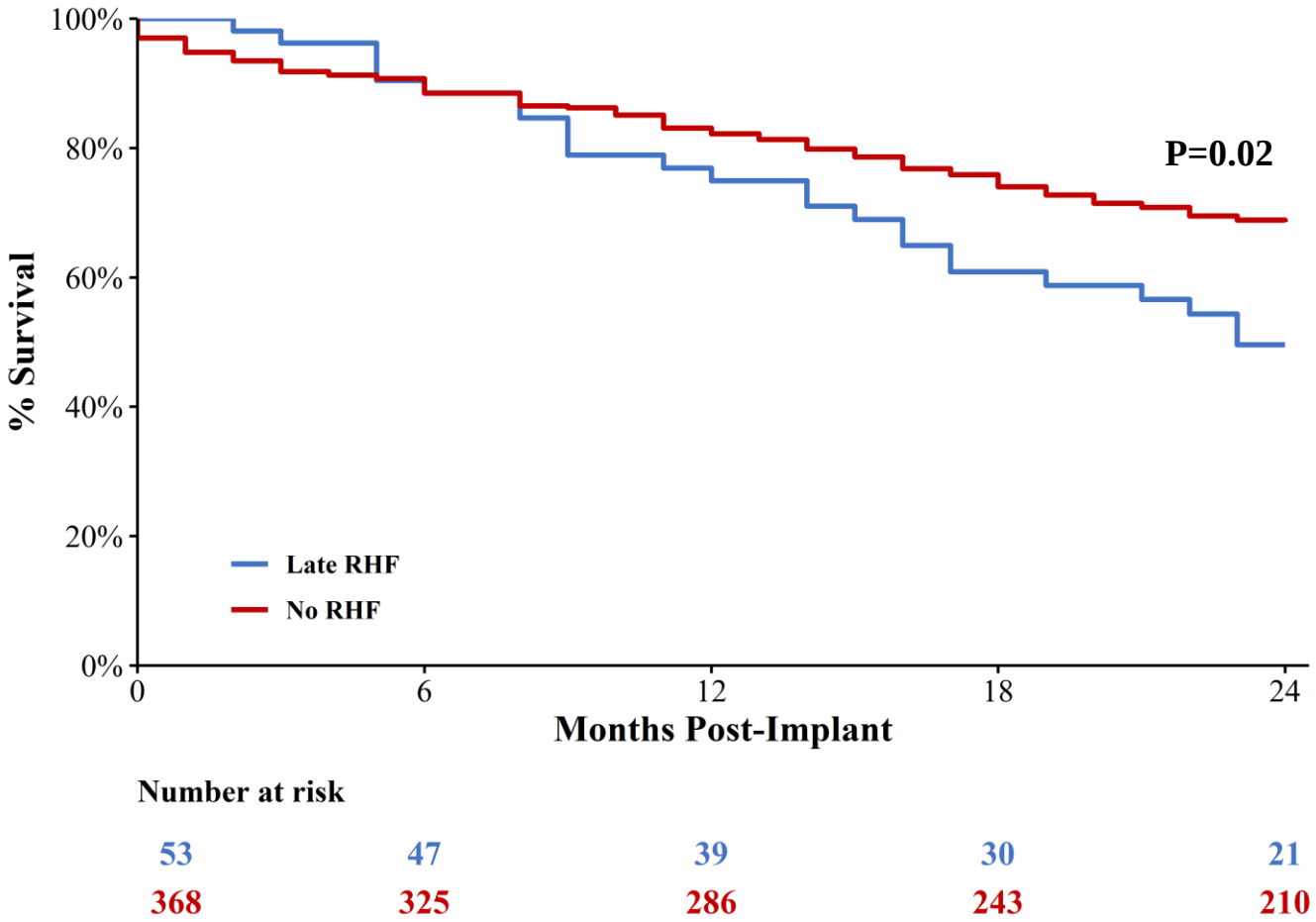
Results

Kaplan-Meier Survival (Late RHF vs No RHF) – Conditional on Discharge



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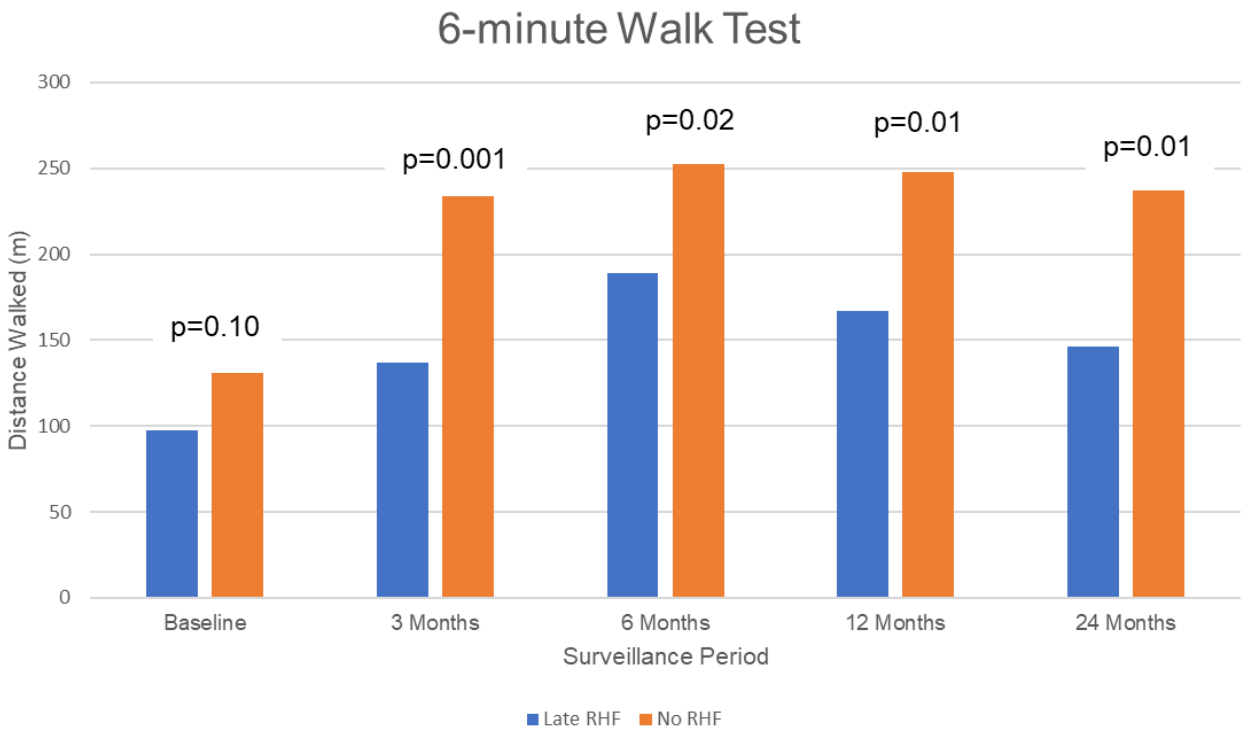
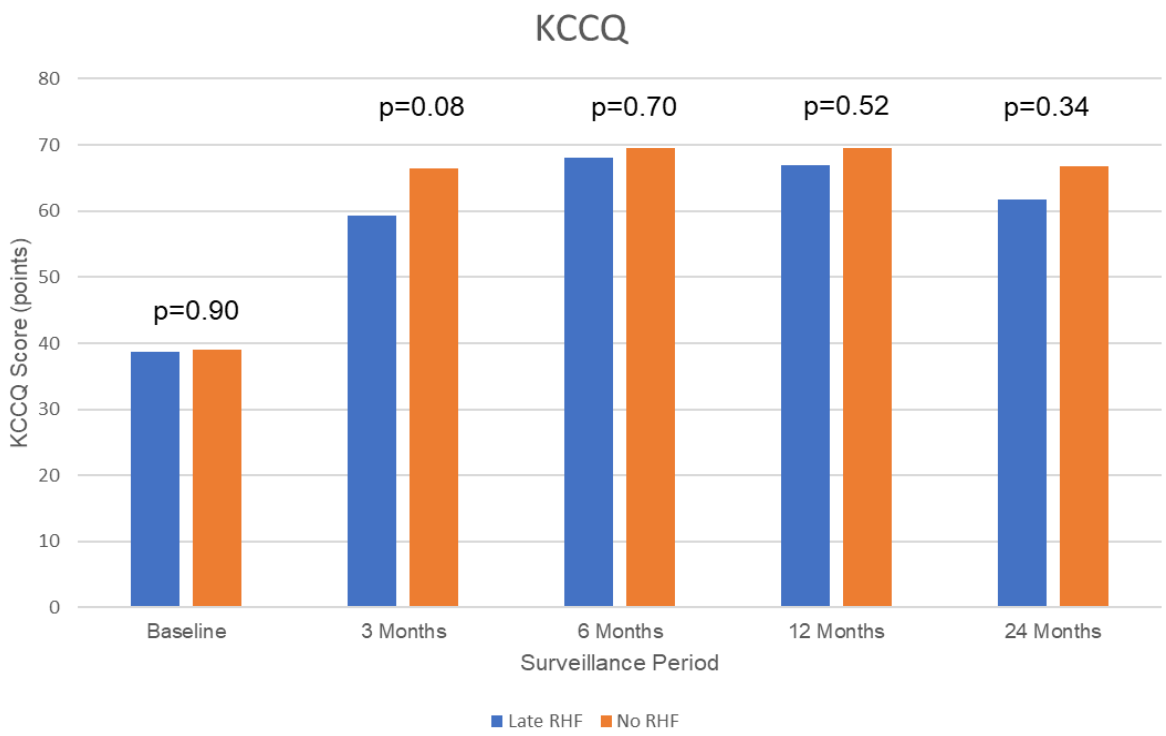
Results

Functional Capacity and Quality of Life (Late RHF vs No RHF)





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Limitations

- Retrospective review
- Narrow definition of RHF
  - RVAD
  - iNO > 1 week
  - Inotropes > week
- No data on hospitalizations for RHF that did not meet these definitions, so the prevalence of milder degrees of LRHF could not be assessed.
- Associations with outcomes are univariate

Conclusions

- Late RHF portends significant morbidity and mortality in destination therapy LVAD patients
- Baseline risk factors for LRHF include increased BMI and decreased pulmonary pressure index and was associated with a longer VAD implant admission.
- Late RHF, as defined by this study, was relatively rare occurrence, but is significantly associated with increased rehospitalizations, reduced survival, decreased functional capacity, and adverse events such as hepatic dysfunction, acute renal failure, sepsis, and respiratory failure.

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THANK YOU

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